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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/648,994	MILLER ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 06/07/07 and 03/13/07 in response to the non-final Office Action mailed 09/11/06. With these, Applicants have amended the specification and the claims.

Status of Claims

2) Claims 1 and 3 have been amended via the amendment filed 03/13/07.

Claims 1-20 are pending.

Claims 1-10 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the specification made in paragraph 6 of the Office Action mailed 09/11/06 is withdrawn in light of Applicants' amendments to the specification.

Rejection(s) Withdrawn

6) The rejection of claim 1 and those dependent therefrom made in paragraph 8 of the Office Action mailed 09/11/06 under 35 U.S.C. § 101 because the claimed invention as being directed to non-statutory subject matter, is withdrawn in light of Applicants' amendment to claim 1.

7) The rejection of claims 6, 7, 9 and 10 made in paragraph 10(a) of the Office Action mailed 09/11/06 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

8) The rejection of claim 3 made in paragraph 10(b) of the Office Action mailed 09/11/06 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

9) The rejection of claims 1 and 6 made in paragraph 12 of the Office Action mailed 09/11/06 under 35 U.S.C § 102(b) as being anticipated by Ruedl *et al.* (*Vaccine* 14: 792-798, 1996), is withdrawn in light of Applicants' amendment to the base claim. A new/modified rejection is set forth below to address the claims, as amended. Applicant's arguments with respect to Ruedl *et al.* have been considered but are moot in view of the withdrawal of, or the new ground(s) of rejection.

10) The rejection of claims 1, 6 and 7 made in paragraph 13 of the Office Action mailed 09/11/06 under 35 U.S.C § 102(e)(1) as being anticipated by Mason *et al.* (US 2003/0176653 A1, already of record), is withdrawn in light of Applicants' amendment to the base claim.

Claim Interpretation

11) As amended currently, the native *E. coli* LT in the base claim 1 is required to be isolated and be present as an adjuvant, and the claimed composition is required not to produce 'any pathogenic effects in the vaccinated bird'. The limitation 'isolated ....LT' lacks a structure and/or size limit, and is not required to be an isolated LT holotoxin, and therefore encompasses LT holotoxin, B subunit or A subunit of *E. coli* LT. The broad limitation 'the vaccinated bird' is not required to be a bird vaccinated with the claimed composition, but encompasses a bird vaccinated with any generic vaccine.

New Rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

12) Claim 1 and those claims dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1, as amended currently, includes the new limitations: 'isolated' native *E. coli* heat-labile toxin (LT) 'as an adjuvant' for use in vaccinating a bird and the negative limitation

'wherein the composition does not produce any pathogenic effects in the vaccinated bird'. Applicants do not point to specific parts of the specification that support the newly added limitations, including the negative limitation or the generic 'the vaccinated bird'. The instant application does appear to provide descriptive support for the above-identified limitations and the now-claimed scope of the claim(s). Therefore, the above-identified new limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed by pointing to specific lines and pages, for the new limitations, or alternatively, to remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 102

13) Claims 1-3, 6 and 7 are rejected under 35 U.S.C § 102(b) as being anticipated by Rice *et al.* (*In: Abstracts of the Workshop on Campylobacters, Helicobacters and Related Organisms.* Vol. 8: abstract 2-31, pages 408-409, 1995).

Rice *et al.* taught a composition comprising 25 or 50 micrograms of an isolated native *E. coli* heat-labile toxin (LT) adjuvant along with a *Campylobacter* vaccine (i.e., immunoprotective antigen effective in a bird) for oral administration to broiler chickens. While the abstract reported a significant reduction in caecal colonization by *Campylobacter jejuni* in vaccinated chickens, the abstract does not report any pathogenic effects in the vaccinated chickens. See entire abstract. The limitation in claim 7, 'produced by a transgenic plant', is a process limitation in a product claim. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art native LT differs from that of the instantly claimed native LT.

Claims 1-3, 6 and 7 are anticipated by Rice *et al.*

14) Claims 1, 6 and 7 are rejected under 35 U.S.C § 102(b) as being anticipated by Beignon *et al.* (*Immunology* 102: 344-351, March 2001).

The limitation 'for use in vaccinating a bird' represents the intended use of the claimed product and therefore has no patentable weight.

Beignon *et al.* taught a composition comprising sterile saline and 25, 50 or 100 micrograms of native *E. coli* LT, with or without an additional protein, and another composition comprising sterile saline and 50 micrograms of native *E. coli* LT, with or without a heterologous viral antigen, for immunization purposes. See 'Materials and Methods' including the paragraph bridging the two columns on page 345; first full paragraph in right column on page 345; Results on page 346; Figures 1, 4 and 5; Table 1; and second full paragraph in left column on page 348. The LT exerted an adjuvant effect on the co-administered antigen in addition to inducing a protective anti-LT response. See paragraph bridging pages 348 and 349; and first two paragraphs under 'Discussion'. Since Beignon's LT dose of 25, 40, 50 or 100 micrograms is the same dose of LT administered by Applicants in the instant specification (see sections [0055] and [0061]), Beignon's composition is expected to necessarily cause no pathogenic effects in vaccinated birds, or birds vaccinated therewith. The limitation in claim 7, 'produced by a transgenic plant', is a process limitation in a product claim. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art native LT differs from that of the instantly claimed native LT.

Claims 1, 6 and 7 are anticipated by Beignon *et al.*

15) Claims 1, 6 and 7 are rejected under 35 U.S.C § 102(b) as being anticipated by Gluck *et al.* (*J. Infect. Dis.* 181: 1129-1132, March 2000).

The limitation 'for use in vaccinating a bird' in claim 1 represents the intended use of the claimed product and therefore has no patentable weight.

Gluck *et al.* taught a vaccine composition comprising 2 micrograms per dose of native *E. coli* heat-labile toxin (HLT) produced by an *E. coli* strain and/or a heterologous viral antigen. The native HLT in the heterologous antigen-containing composition augmented the immune response to the HA antigen and also induced a significant HLT-specific immune response. Gluck *et al.* particularly taught that small quantities of native HLT can be safely administered. See abstract; paragraph bridging 1129 and 1130; and 'Discussion' including the last paragraph. That the prior art composition does not produce any pathogenic effects in a bird vaccinated with the composition is inherent from the teachings of Gluck *et al.* since the 2 micrograms of the native *E. coli* heat-labile toxin (HLT) contained therein is within the quantity of 10 micrograms used by Applicants in the instant application (see Table 7). The limitation in claim 7, 'produced by a transgenic plant', is a process limitation in a product claim. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the

alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art native LT differs from that of the instantly claimed native LT.

Claims 1, 6 and 7 are anticipated by Gluck *et al.*

16) Claims 1, 6 and 7 are rejected under 35 U.S.C § 102(b) as being anticipated by Arntzen *et al.* (US 6,194,560, already of record).

Arntzen *et al.* disclosed a native *E. coli* LT holotoxin composition wherein the native LT is produced in transformed or transgenic plants by stable or transient incorporation of DNA coding for an LT-B protein *and* an LT-A protein, wherein the plant-produced LT holotoxin acts as even a better adjuvant for enhanced secretory immune response in some circumstances. Fusion proteins produced in transgenic plants comprising fused LT holotoxin, wherein one or more antigenic or immunogenic agents from a pathogenic microorganism are expressed that are sufficient to immunize an animal (bird included) against the immunogenic agents on administration thereto, are taught. See column 17 including first and third paragraphs; column 18 including full paragraphs 3-4 and 1; and Example 3. Arntzen's LT holotoxin enterotoxin is a protein produced by enterotoxic *E. coli* or transgenic organisms containing the gene for LT-A and LT-B. See fifth full paragraph in column 12. Arntzen's LT fusion protein is a protein where both LT-a and LT-B subunits of the LT toxin further include other antigenic proteins such that the LT-A protein associates with the pentameric B subunit to form the intact holotoxin in the unmodified (native) form. See paragraph bridging columns 12 and 13. Arntzen's invention provides for the coexpression of both the LT-A *and* LT-B subunits so that the holotoxin is assembled in the plant tissues to act both as an adjuvant and an immunogen, and to coprovide other viral antigens. See first full paragraph in column 14. Arntzen's isolated LT holotoxin is produced in transgenic potato plants expressing both LT-A and LT-B within the same cells of tuber tissue. See Examples 17 and 18.

Claims 1, 6 and 7 are anticipated by Arntzen *et al.*

17) Claims 1-5 and 7-10 are rejected under 35 U.S.C § 102(b) as being anticipated by Arntzen *et al.* (US 6,194,560, already of record) as evidenced by Pal *et al.* (US 7,186,560).

Since the limitation 'LT' is not required to be an LT holotoxin, it is interpreted in this rejection as encompassing LT-B.

Arntzen *et al.* disclosed a composition or tuber slurry composition comprising 2.5 to 10 micrograms per dose of native LT-B adjuvant expressed in transgenic potato tubers along with a heterologous viral antigen, such as, Newcastle disease virus antigen. The composition enhanced the immune response of birds immunized therewith to Newcastle disease virus and elicited NDV hemagglutinin-inhibiting antibodies and also LT-B-specific antibodies as well. See Example 29; column 45; and Tables 8 and 9. Arntzen *et al.* taught an isolated LT holotoxin produced in transgenic potato plants expressing both LT-B and LT-A (i.e., immunoprotective antigen) within the same cells of tuber tissue. See Examples 17 and 18. That the prior art LT-B composition does not produce pathogenic effects in vaccinated birds is inherent from the teachings of Arntzen *et al.* in light of what is known in the art. For instance, Pal *et al.* teach that LT-B is the non-toxic B subunit of *E. coli* heat-labile toxin of ETEC *E. coli*. See section Example 6.

Claims 1-5 and 7-10 are anticipated by Arntzen *et al.* The reference of Pal *et al.* is not used as a secondary reference in combination with Arntzen *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Arntzen *et al.* with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

Relevant Art

18) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

♦ LaFayette *et al.* (*In: Plant Biology. Annual Meeting of the American Society of Plant Physiologists.* San Diego, California, abstract 661, page 138, July 15-19, 2000) taught the transformed soybeans expressing the Newcastle Disease Virus P and F genes, the avian influenza HA5 gene, and the infectious bronchitis virus S1 glycoprotein gene for immunization of poultry with the plant-synthesized viral proteins. See entire document.

Remarks

19) Claims 1-10 stand rejected.

It is noted that claim 4 includes the misspelled limitation 'avain'. See line 3.

20) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time

policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted to the Office' Central Rightfax number 571-273-8300 via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week.

22) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

23) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

July, 2007

S. DEVI, PH.D.
PRIMARY EXAMINER